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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	6

DATE MAILED: 10/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/548,290	Applicant(s) SASAKAWA ET AL.	
	Examiner Anne M Beckerleg	Art Unit 1632	

-- The MAILING DATE of this communication appears on th cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response to the restriction/election received on 7/6/01 has been entered. Applicant's election with traverse of group I, claims 1-16 and 18-19 is acknowledged. Applicant's further election with traverse of the species atopic dermatitis for group I is acknowledged. Claims 17 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5. Claims 1-16 and 18-19 are currently under examination in the instant application. An action on the merits follows.

Election/Restriction

Applicant's election with traverse of group I and the species atopic dermatitis in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the office has not provided sufficient reasons why group I and II and the identified species are patentably distinct. The previous office action, however stated, that the inventions are distinct, each from the other because of the following reasons: the methods of treating or preventing allergy using an agent of Invention II differ substantially in methodology and reagent use than the methods of screening agents in an animal model of allergy or the animal model of allergy of Invention I. Further, the agent of Invention II may be identified or made without using the instant screening method of Invention I,

such as by testing agents *in vitro*. It is also noted that the animal model itself does not require the agent for its production or use. Thus, the office provided substantial reasons why the inventions of group two are separate and distinct. Further, the search for invention I is not co-extensive with the search for invention II and as such, it would present an undue burden on the examiner to search and examine both inventions.

The applicant also states that MPEP 803 discloses that is a product is found allowable, withdrawn process claims which depend from the product will be rejoined. This is not relevant to the instant application as the "agent correlated with an allergy symptom" used in the methods of group II has not been claimed by the applicants as a product.

In regards to the election of species requirement. The diseases disclosed and claimed by the applicants are patentably distinct in that they have substantially different symptoms and etiologies and are caused by different genetic defects or exposures to substantially different types of antigens. The applicant is reminded that should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Thus, applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds for restriction. This requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, and 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mouse model of atopic dermatitis comprising an NC/nga mouse raised under specific pathogen free conditions which has been exposed to a mite or mite extract, and methods of using said mouse model to screen for therapeutic agents effective against atopic dermatitis, does not reasonably provide enablement for the generation of any type of animal model for atopic dermatitis which comprises the exposure of any type of animal under specific pathogen free conditions to any allergen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification discloses that the NC/nga mouse raised under conventional conditions spontaneously develops skin lesions resembling atopic dermatitis in humans, whereas NC/nga mice raised under specific pathogen free conditions do not. The specification further discloses and provides working examples which demonstrate that NC/nga mice raised under specific pathogen free conditions can develop atopic dermatitis like symptoms when exposed to mite antigen extracts.

The specification does not provide sufficient guidance as to animal strains which are capable of developing symptoms resembling those observed in human atopic dermatitis patients in response to a mite antigen or any other type of allergen. While the specification states generally that "immuno-modulated" animals can be used in the instant methods, the specification does not provide sufficient guidance as to what constitutes an "immuno-modulated" animal, see also the rejection of the claims under 35 U.S.C. 112, second paragraph, below. The term immunomodulated suggests that the animals have either been treated with an immunomodulating agent or are naturally or genetically engineered to have altered immune responses. The specification fails to disclose how to make a genetically engineered "immuno-modulated" animal or provide guidance as to methods and reagents useful for producing an "immuno-modulated" animal capable of developing atopic dermatitis like symptoms. As to the animal strains listed in the specification, it is noted that the art does not teach that any of these strains other than the MRL/lpr mouse has any specific immunological defects, or that any of these strains exhibit atopic dermatitis like symptoms either spontaneously or in response to an allergen. The specification's

working examples are further limited to the use of NC/nga mice, and do not demonstrate that any other animal is capable of developing a condition resembling atopic dermatitis. It is also noted that at the time of filing, only the NC/nga mouse had been disclosed in the art as a model for atopic dermatitis. In regards to other mouse strains, the art at the time of filing teaches that other mouse strains, such as the A/J mouse, while capable of generating antibodies against mite allergens, did not the develop skin lesions associated with atopic dermatitis that are observed in the NC/nga following spontaneous dermatitis development or following mite exposure (see for instance Yasue et al. (1997) Cell. Immunol., Vol. 181, 30-37). Thus, based on the teachings of the art at the time of filing, it would appear that the NC/nga mouse is unique in being capable of developing, either spontaneously or as a result of mite exposure, symptoms which resemble atopic dermatitis in humans. Therefore, in view of the apparent uniqueness of the NC/nga strain of mice in being able to develop symptoms which resemble atopic dermatitis in humans, the lack of guidance in the specification as to how to make "immuno-modulated" animals which share the same characteristics as the NC/nga mouse or which are capable of developing atopic dermatitis like symptoms in response to an allergen, the teachings in the art that other mouse strains besides the NC/nga strain do not develop atopic dermatitis like symptoms in response to mite extract, the limitation of the working examples to NC/nga mice, and the breadth of the claims, it would have required undue experimentation for the skilled artisan to make or use the encompassed animals as claimed.

The specification does not provide an enabling disclosure for producing symptoms of atopic dermatitis in specific pathogen free NC/nga mice using any allergen other than a mite or mite extract. The art at the time of filing teaches that NC/nga mice when raised under conventional conditions spontaneously develop skin lesions. The art speculates that this reaction in the NC/nga mice is caused by environmental antigens. The art further teaches that humans with atopic dermatitis exhibit extreme hypersensitivity to mite antigens, and that the exposure of specific pathogen free NC/nga mice to mites results in skin lesions. At the time of filing, the art had not identified any other environmental antigen associated with the development of atopic dermatitis. The specification fails to provide any additional information as to the identity or characteristics of any other allergen other than a mite which is implicated or been demonstrated with the atopic dermatitis. In the absence of any disclosure by the specification or the prior art, the skilled artisan would not have any idea which of the innumerable potential environmental antigens might be responsible for generating atopic dermatitis like symptoms in NC/nga mice. Further, the applicant is reminded that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991). Thus, based on the unknown nature of the allergens responsible for the development of spontaneous atopic dermatitis like symptoms in NC/nga mice, the limitation of the specification's disclosure and working examples to mite allergens, and the breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 and 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The applicant's claims recite the term "immuno-modulated" animal. It is unclear what the metes and bounds are of the term "immuno-modulated". The specification states that immuno-modulated animals are known in the art and recites several specific examples. The examples listed represent various strains and substrains of mice. While the MRL/lpr mouse does in fact have an immune deficiency, the art does not report that the LEC rat, or NZW/B F1 mouse for instance have any specific immune defects. Thus, it is unclear what types of animals would qualify as "immuno-modulated". It is also unclear whether the claims are meant to include animals which have been genetically manipulated or have been exposed to immune modulating substances. Therefore, the term "immuno-modulated" as used in the instant claims, is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Morita et al. (1999), J. Derm. Science., Vol. 19, 37-43. The applicant claims an animal model for atopic dermatitis which is an immuno-modulated animal which has been sensitized with an antigen under specific pathogen free environment such that the animal displays allergy symptoms caused by the antigen. The applicant further claims said animal model which is an NC/Nga mouse and wherein the allergen is a mite. The applicant also claims methods of making said animal model comprising maintaining the animal in a Specific Pathogen Free environment and sensitizing the animal with the antigen for at least 5 days.

Morita et al. teaches NC mice, an inbred strain of fancy mice established in 1955, which have been bred under specific pathogen free conditions and renamed NC/kuj. It is noted that NC mice bred under regular conditions are typically referred to as NC/Nga mice and are further known to spontaneously develop allergic symptoms which resemble atopic dermatitis (Morita et al., page 38, column 1). Morita et al. further teaches the exposure of specific pathogen free NC mice to fur mites for two weeks, wherein the fur mite exposure results in skin lesions resembling those associated with atopic dermatitis and anti-mite IgE production (Morita et al., page 39, and page 41). Morita concludes that specific pathogen free NC mice exposed to mite antigen represent a mouse model for atopic dermatitis (Morita et al., page 42, column 2). Thus, by teaching all the limitations of the claims, Morita et al. anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morita et al. (1999), J. Derm. Science., Vol. 19, 37-43 in view of Yasue et al. (1997) Cell. Immunol., Vol. 181, 30-37. The applicant claims an animal model for atopic dermatitis which is an immuno-modulated NC/nga mouse which has been sensitized with a mite extract under specific pathogen free environment such that the animal displays allergy symptoms caused by the antigen.

Morita et al. teaches NC mice, an inbred strain of fancy mice established in 1955, which have been bred under specific pathogen free conditions and renamed NC/kuj. It is noted that NC mice bred under regular conditions are typically referred to as NC/Nga mice and are further

known to spontaneously develop allergic symptoms which resemble atopic dermatitis (Morita et al., page 38, column 1). Morita et al. further teaches the exposure of specific pathogen free NC mice to fur mites for two weeks, wherein the fur mite exposure results in skin lesions resembling those associated with atopic dermatitis and anti-mite IgE production (Morita et al., page 39, and page 41). Morita concludes that specific pathogen free NC mice exposed to mite antigen represent a mouse model for atopic dermatitis (Morita et al., page 42, column 2).

While Morita et al. teaches how to make a mite extract, see page 38, column 2, paragraph 4, Morita et al. does not specifically teach administering a mite extract rather than live mites to specific pathogen free NC mice in order to produce a mouse model for atopic dermatitis. Yasue et al. supplements Morita by teaching that the administration of mite extract to generate allergic responses in mice is a standard procedure (Yasue et al., page 30, column 2, and page 32). It is further noted that the skilled artisan would be motivated to use a mite extract over live mites in order to standardize the amount of antigen to which each mouse is exposed, thereby ensuring a homogenous population of exposed mice. Thus, in order to produce a more homogeneous population of mite sensitized mice for use as an animal model of human allergic disease, it would have been *prima facie* obvious to the skilled artisan to substitute mite extract injection as taught by Yasue et al. for the live mite exposure taught by Morita et al. in the method of producing a murine model of atopic dermatitis taught by Morita et al. Further, based on the successful use of mite extracts to generate allergic responses in mice as taught by Yasue et al., the skilled artisan

would have had a reasonable expectation of success in generating a mouse model of atopic dermatitis by exposing specific pathogen free NC mice to a mite extract.

Claims 15-16 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morita et al. (1999), J. Derm. Science., Vol. 19, 37-43 in view of Hiroi et al. (1998) Jpn. J. Pharmacol., Vol. 76, 175-183. The applicant claims methods of screening for an agent effective against atopic dermatitis or useful for preventing atopic dermatitis comprising applying at least one agent to an animal which has been exposed to an antigen under specific pathogen free conditions and determining whether the agent reduces or prevents allergy symptoms.

Morita et al. teaches NC mice, an inbred strain of fancy mice established in 1955, which have been bred under specific pathogen free conditions and renamed NC/kuj. It is noted that NC mice bred under regular conditions are typically referred to as NC/Nga mice and are further known to spontaneously develop allergic symptoms which resemble atopic dermatitis (Morita et al., page 38, column 1). Morita et al. further teaches the exposure of specific pathogen free NC mice to fur mites for two weeks, wherein the fur mite exposure results in skin lesions resembling those associated with atopic dermatitis and anti-mite IgE production (Morita et al., page 39, and page 41). Morita concludes that specific pathogen free NC mice exposed to mite antigen represent a mouse model for atopic dermatitis (Morita et al., page 42, column 2).

While Morita et al. teaches how to make a mite extract, see page 38, column 2, paragraph 4, Morita et al. does not specifically teach administering a mite extract rather than live mites to

specific pathogen free NC mice in order to produce a mouse model for atopic dermatitis. Yasue et al. supplements Morita by teaching that the administration of mite extract to generate allergic responses in mice is a standard procedure (Yasue et al., page 30, column 2, and page 32). It is further noted that the skilled artisan would be motivated to use a mite extract over live mites in order to standardize the amount of antigen to which each mouse is exposed, thereby ensuring a homogenous population of exposed mice. Thus, in order to produce a more homogeneous population of mite sensitized mice for use as an animal model of human allergic disease, it would have been *prima facie* obvious to the skilled artisan to substitute mite extract injection as taught by Yasue et al. for the live mite exposure taught by Morita et al. in the method of producing a murine model of atopic dermatitis taught by Morita et al. Further, based on the successful use of mite extracts to generate allergic responses in mice as taught by Yasue et al., the skilled artisan would have had a reasonable expectation of success in generating a mouse model of atopic dermatitis by exposing specific pathogen free NC mice to a mite extract.

Morita et al., while suggesting that specific pathogen free NC mice exposed to mites represent a mouse model for atopic dermatitis, does not specifically teach using these mice to test for therapeutic compounds effective against atopic dermatitis. However, it is noted that Morita et al. does teach that the administration of ivermectin to the mice reduces anti-mite IgE levels and skin lesions (Morita et al., pages 41-42). This demonstrates that the mice are suitable for testing potential therapeutic agents. Hiroi et al. further supplements Morita et al. by providing motivation for testing potential therapeutic agents in mouse models of atopic dermatitis. Hiroi teaches that

the standard model for spontaneous atopic dermatitis, NC mice raised under conventional and not specific pathogen free conditions, can be used to screen for therapeutic agents. Specifically, Hiroi teaches that FK506 ointment, not betamethasone valerate ointment, was determined to be effective in suppressing and inhibiting symptoms of atopic dermatitis when applied to NC mice both before and after the development of dermatological symptoms (Hiroi et al., page 176 and Figure 1, 2, and 3). Thus, in view of the motivation provided by Hiroi et al. for using murine models of atopic dermatitis to determine the effectiveness of agents in preventing or inhibiting atopic dermatitis, it would have been *prima facie* obvious to use the screen agents for effectiveness against atopic dermatitis using the mouse model taught by Morita et al. Further, based on the demonstration by Morita et al. that ivermectin is useful for treating atopic dermatitis like symptoms in the mouse model of atopic dermatitis developed by Morita et al., the skilled artisan would have had a reasonable expectation of success in testing agents for effectiveness against atopic dermatitis using the mouse model taught by Morita et al.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Beckerleg, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Karen Hauda, can be reached at (703) 305-6608. General inquiries should

be directed to the group receptionist whose phone number is (703) 308-0196. The official fax number is (703) 308-4242.

Dr. A.M.S. Beckerleg

A.M.S. BECKERLEG
PATENT EXAMINER